<u>What is claimed is:</u>

1.   A method to select a cancer patient who is predicted to benefit from therapeutic administration of an EGFR inhibitor, an agonist thereof, or a drug having substantially similar biological activity as EGFR inhibitor, comprising:

5   a)   providing a sample of tumor cells from a patient to be tested;

             b)   detecting in the sample the expression of one or more genes chosen from a panel of genes whose expression has been correlated with sensitivity or resistance to an EGFR inhibitor;

             c)   comparing the level of expression of the gene or genes detected in

10   the patient sample to a level of expression of the gene or genes that has been correlated with sensitivity or resistance to the EGFR inhibitor; and

             d)   selecting the patient as being predicted to benefit from therapeutic administration of the EGFR inhibitor, if the expression of the gene or genes in the patient's tumor cells is statistically more similar to the expression levels of the

15   gene or genes that has been correlated with sensitivity to the EGFR inhibitor than to resistance to the EGFR inhibitor.

2.   The method of Claim 1, wherein the panel of genes in (b) is identified by a method comprising:

             a)   providing a sample of cells that are sensitive or resistant to

20   treatment with the EGFR inhibitor;

             b)   detecting the expression of at least one gene in the EGFR inhibitor-sensitive cells as compared to the level of expression of the gene or genes in the EGFR inhibitor-resistant cells; and

             c)   identifying a gene or genes having a level of expression in EGFR

25   inhibitor-sensitive cells that is statistically significantly different than the level of expression of the gene or genes in EGFR inhibitor-resistant cells, as potentially being a molecule that interacts with the EGFR pathway to allow or enhance responsiveness to EGFR inhibitors.

3.   The method of Claim 1, wherein the EGFR inhibitor is gefitinib.

30   4.   The method of Claim 3, wherein step (b) comprises detecting in the sample the expression of one or more genes chosen from a gene comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194;

wherein step (c) comprises comparing the level of expression of the gene or genes detected in the patient sample to a level of expression of the gene or genes that has been correlated with sensitivity or resistance to gefitinib; and

wherein step (d) comprises selecting the patient as being predicted to benefit from therapeutic administration of gefitinib, an agonist thereof, or a drug having substantially similar biological activity as gefitinib, if the expression of the gene or genes in the patient's tumor cells is statistically more similar to the expression levels of the gene or genes that has been correlated with sensitivity to gefitinib than to resistance to gefitinib.

5.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least two genes in (b).

6.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least three genes in (b).

7.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least four genes in (b).

8.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least five genes in (b).

9.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least 10 genes in (b).

10.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least 25 genes in (b).

11.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least 50 genes from in (b).

12.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least 100 genes in (b).

13.   The method of Claim 1 or Claim 4, wherein the step (b) of detecting comprises detecting expression of at least 150 genes in (b).

14.   The method of Claim 1, wherein the step (b) of detecting comprises detecting expression of substantially all of the genes in the panel of genes.

15.   The method of Claim 4, wherein step (b) of detecting comprises detecting substantially all of the genes in (b).

16.   The method of any one of Claims 1-15, wherein expression of the gene or genes is detected by measuring amounts of transcripts of the gene in the tumor cells.

17.   The method of any one of Claims 1-15, wherein expression of the gene or genes is detected by detecting hybridization of at least a portion of the gene or a transcript thereof to a nucleic acid molecule comprising a portion of the gene or a transcript thereof in a nucleic acid array.

18.   The method of any one of Claims 1-15, wherein expression of the gene is detected by detecting the production of a protein encoded by the gene.

19.   The method of any one of Claims 1-15, comprising detecting expression of at least one gene selected from the group consisting of: E-cadherin (represented by SEQ ID NO:3) and ErbB3 (represented by SEQ ID NO:15 or SEQ ID NO:133).

20.   The method of any one of Claims 1-15, further comprising detecting expression of at least one gene selected from the group consisting of ZEB1 and SIP1.

21.   The method of any one of Claims 1-15, comprising comparing the expression of the gene or genes to expression of the gene or genes in a cell from a non-cancerous cell of the same type.

22.   The method of any one of Claims 1-15, comprising comparing the expression of the gene or genes to expression of the gene or genes in an autologous, non-cancerous cell from the patient.

23.   The method of any one of Claims 1-15, comprising comparing the expression of the gene or genes to expression of the gene or genes in a control cell that is resistant to the EGFR inhibitor.

24.   The method of any one of Claims 1-15, comprising comparing the expression of the gene or genes to expression of the gene or genes in a control cell that is sensitive to the EGFR inhibitor.

25.   The method of any one of Claims 1-15, wherein control expression levels of the gene or genes that has been correlated with sensitivity and/or resistance to the EGFR inhibitor has been predetermined.

26.   A method to identify molecules that interact with the EGFR pathway to allow or enhance responsiveness to EGFR inhibitors, comprising:

a)   providing a sample of cells that are sensitive or resistant to treatment with gefitinib;

b)   detecting the expression of at least one gene in the gefitinib-sensitive cells as compared to the level of expression of the gene or genes in the gefitinib-resistant cells; and

c)   identifying a gene or genes having a level of expression in gefitinib-sensitive cells that is statistically significantly different than the level of expression of the gene or genes in gefitinib-resistant cells, as potentially being a molecule that interacts with the EGFR pathway to allow or enhance responsiveness to EGFR inhibitors.

27.   A plurality of polynucleotides for the detection of the expression of genes that are indicative of sensitivity or resistance to gefitinib, an agonist thereof, or a drug having substantially similar biological activity as gefitinib;

wherein the plurality of polynucleotides consists of at least two polynucleotides, wherein each polynucleotide is at least 5 nucleotides in length, and wherein each polynucleotide is complementary to an RNA transcript, or nucleotide derived therefrom, of a gene that is regulated differently in gefitinib-sensitive tumor cells as compared to gefitinib-resistant cells.

28.   The plurality of polynucleotides of Claim 27, wherein each polynucleotide is complementary to an RNA transcript, or a polynucleotide derived therefrom, of a gene comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194.

29.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least two genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194.

30.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least five genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194.

31.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least 10 genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194.

32.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least 25 genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ
5   ID NOs:1-194.

33.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least 50 genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ
10   ID NOs:1-194.

34.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least 100 genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ
15   ID NOs:1-194.

35.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of at least 150 genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ
20   ID NOs:1-194.

36.   The plurality of polynucleotides of Claim 27, wherein the plurality of polynucleotides comprises polynucleotides that are complementary to an RNA transcript, or a nucleotide derived therefrom, of all of the genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ
25   ID NOs:1-194.

37.   The plurality of polynucleotides of any one of Claims 27-36, wherein said polynucleotide probes are immobilized on a substrate.

38.   The plurality of polynucleotides of any one of Claims 27-36, wherein said polynucleotide probes are hybridizable array elements in a microarray.

30   39.   The plurality of polynucleotides of any one of Claims 27-36, wherein said polynucleotide probes are conjugated to detectable markers.

40.   A plurality of antibodies, antigen binding fragments thereof, or antigen binding peptides, for the detection of the expression of genes that are indicative of

56

sensitivity or resistance to gefitinib, an agonist thereof, or a drug having substantially similar biological activity as gefitinib;

wherein said plurality of antibodies, antigen binding fragments thereof, or antigen binding peptides consists of at least two antibodies, antigen binding fragments thereof, or antigen binding peptides, each of which selectively binds to a protein encoded by a gene comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194.

41.   A method to identify a compound with the potential to enhance the efficacy of EGFR inhibitors, comprising:

a)   contacting a test compound with a cell that expresses at least one gene, wherein said gene is selected from any one of the genes comprising, or expressing a transcript comprising, a nucleic acid sequence selected from the group consisting of SEQ ID NOs:1-194;

b)   identifying compounds selected from the group consisting of:

i)   compounds that increase the expression or activity of the gene or genes in (a), or the proteins encoded thereby, that are correlated with sensitivity to gefitinib; and

ii)   compounds that decrease the expression or activity of genes in (a), or the proteins encoded thereby, that are correlated with resistance to gefitinib;

wherein said compounds are identified as having the potential to enhance the efficacy of EGFR inhibitors.

42.   The method of Claim 41, wherein the cell expresses a gene encoding E-cadherin or ErbB3, and wherein step (b) comprises identifying compounds that increase the expression or activity of E-cadherin or ErbB3 or the gene encoding E-cadherin or ErbB3.

43.   The method of Claim 41, wherein the cell expresses a gene encoding ZEB1 and SIP1, wherein step (b) comprises identifying compounds that decrease the expression or activity ZEB1 or SIP1 or the gene encoding ZEB1 or SIP1.

44.   A method to treat a patient with a cancer, comprising administering to the patient a therapeutic composition comprising a compound identified by the method of Claim 41.

45.   A method to treat a patient with a cancer, comprising administering to the patient a therapeutic composition comprising a compound that upregulates the expression or activity of E-cadherin or ErbB3 or the gene encoding E-cadherin or ErbB3 in the tumor cells of the patient.

46.   A method to treat a patient with a cancer, comprising administering to the patient a therapeutic composition comprising a compound that downregulates the expression of ZEB1 or SIP1 or the gene encoding ZEB1 or SIP1 in the tumor cells of the patient.